

## II. Remarks

After entry of the amendment, claims 2-8, 10-17, 19-31, 33-40 and 104-107 are pending.

Claims 2 and 107 have been amended, and are supported by the specification, at for example, page 4, lines 1-6; page 22 (e.g., Scheme 1); page 24 (e.g., Scheme 2); page 25 (e.g., Scheme 3); and Examples 8-16.

Claim 3 has been editorially amended to correct the antecedent basis with reference to claim 2.

No issues of new matter should arise and entry of the amendment is respectfully requested.

### A. **Rejection under 35 U.S.C. § 102(b)**

Claim 2 is rejected under 35 U.S.C. § 102(b) as obvious over Morozowich (U. S. Patent No. 3,922,293).

Applicants respectfully traverse the rejection and respectfully submit that claim 2 is not anticipated by Morozowich in view of the fact that claim 2 has been amended to recite "with the proviso that the compound of formula (I) has at least one NO group or at least one NO<sub>2</sub> group linked through an oxygen atom, a nitrogen atom or a sulfur atom." In view thereof, Applicants respectfully request that the rejection under § 102(b) be withdrawn.

### B **Rejection under 35 U.S.C. § 103(a)**

Claims 2, 4-8, 14-17 and 107 are rejected under 35 U.S.C. § 103(a) as obvious over Bezuglov (U.S. Patent No. 5,625,083) or Del Soldato (WO 98/58910) in view of Garvey et al (U.S. Patent No. 5,874,437), Garvey et al (U.S. Patent No. 6,579,863) and Bandarage et al (U.S. Patent No. 6,593,347).

Applicants respectfully traverse the rejection and respectfully submit that the presently claimed invention is unobvious over the cited references. As admitted by the Patent Office, Bezuglov and Del Soldato both teach **nitro**prostaglandin compounds (i.e., compounds that contain a –NO<sub>2</sub> group) that are specifically excluded by the proviso in the claims. **None of the cited references disclose or suggest the compounds recited in independent claims 2 or 107.**

Bezuglov and Del Soldato do not disclose or suggest the claimed **nitroso**prostaglandin compounds (i.e., compounds that contain a –NO group). Neither Bezuglov nor Del Soldato provide any motivation to modify the disclosed **nitro**prostaglandin compounds to arrive at the

claimed **nitrosoprostaglandin** compounds of the present invention (i.e., to replace the described  $\text{-NO}_2$  group with the claimed  $\text{-NO}$  group of the invention).

Contrary to the assertion by the Patent Office, Berzuglov does not teach the use of the **nitroprostaglandin** compounds for the treatment of impotence. Berzuglov teaches that the **nitroprostaglandin** compounds can induce one or more multiplicity of biological events. For example, in the abstract at line 6-8, Berzuglov states:

“The novel prostanoids produced herein may be used as vasodilators, antihypertensive cardiovascular agents, bronchodilators, and they may have uses in obstetrics and gynecology.”

At column 7, lines 52-59, Berzuglov states:

“These biological events include platelet aggregation, modulation of smooth muscle stimulation, regulation of blood pressure, regulation of gastric secretion, NOSAC (=non-steroidal anti-inflammatory compound)-induced lesion inhibition, bronchodilation, nasal decongestion, peripheral vascular circulatory improvement, reproduction and fertility control, renal blood flow alteration, regulation of inflammation, and regulation of intraocular pressure.”

Thus Bezuglov does not disclose, suggest or motivate one to use the **nitroprostaglandin** compounds for the treatment of impotence.

Garvey et al (U.S. Patent No. 6,579,863) and Bandarage et al (U.S. Patent No. 6,593,347) are prior art to the present application under § 102(e) because the patents issued after the filing date of the present application. The present application, Garvey et al (U.S. Patent No. 6,579,863) and Bandarage et al (U.S. Patent No. 6,593,347) were all subject to an obligation of assignment and/or were assigned to NitroMed, Inc. at the time each of the inventions was made. Pursuant to 35 USC § 103(c), Garvey et al (U.S. Patent No. 6,579,863) and Bandarage et al (U.S. Patent No. 6,593,347) "shall not preclude patentability" since the subject matter of the claimed invention, Garvey et al (U.S. Patent No. 6,579,863) and Bandarage et al (U.S. Patent No. 6,593,347) "were, at the time the invention was made, owned by the same person [i.e., NitroMed, Inc.] or subject to an obligation of assignment to the same person [i.e., NitroMed, Inc.]." Accordingly, Garvey et al (U.S. Patent No. 6,579,863) and Bandarage et al (U.S. Patent No. 6,593,347) cannot be used by the Patent Office to reject the pending claims.

Garvey '437 describes nitro and nitroso phosphodiesterase inhibitors. Garvey '437 does not disclose or suggest nitro and/or nitroso **prostaglandins** and does not provide any motivation for one to modify the prostaglandins described in Bezuglov or Del Soldato to arrive the presently claimed **nitrosoprostaglandins**.

As the Federal Circuit stated in *Velander v. Garner*, 68 USPQ2d 1769, 1772 (November 2003):

a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success.

The Patent Office has not established either factor as required by the Federal Circuit. The record is devoid of any suggestion to one of ordinary skill in the art that they should make the presently claimed compounds or carry out the claimed methods. Garvey '437 does not suggest that one skilled in the art should modify the prostaglandin compounds described in Bezuglov or Del Soldato by replacing the -NO<sub>2</sub> group described therein with the claimed -NO group. In fact, the phosphodiesterase inhibitors described in Garvey '437 are wholly unrelated in chemical structure and mode of action from the presently claimed prostaglandins. The Patent Office has not provided any reason why one skilled in the art would be motivated to look to the phosphodiesterase inhibitors described in Garvey '437 in order to modify prostaglandins in view of the differences in their chemical structures and modes of action. Again, the mere fact that references can be combined or modified does not render the combination obvious unless the prior art also suggests the desirability of the combination and a reasonable expectation for success. *Velander* at 1772; MPEP § 2143.01.

The Patent Office has done nothing more than select isolated teachings in references and combine them to arrive at a hindsight conclusion of obviousness based on the information described in the Applicants' own specification and claims. The Patent Office has not conducted a proper obviousness analysis, and has not established a *prima facie* case of obviousness based on the cited references. MPEP § 2143.01

Again, the combination of Bezuglov, Del Soldato, and Garvey '437 does not disclose, suggest or provide motivation to make or use the presently claimed **nitrosoprostaglandin** compound or any of the other claimed compounds. In view thereof, Applicants respectfully submit that the presently claimed invention is unobvious over the combination of cited references, and respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

**C. Rejection under 37 CFR § 112, First Paragraph**

Claim 107 is rejected under 37 C.F.R. § 112, first paragraph, as lacking enablement.

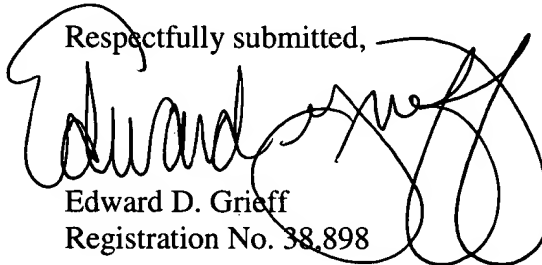
Claim 107 has been amended to recite that the "NO group is linked to the prostaglandin compound through an oxygen atom, a nitrogen atom or a sulfur atom." In view thereof, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

**D. Conclusion**

Applicants respectfully request reconsideration and allowance of claims 2-8, 10-17, 19-31, 33-40 and 104-107.

Examiner Gerstl is encouraged to contact the undersigned at 202-942-8453 concerning any questions about the present application.

Respectfully submitted,



Edward D. Grieff  
Registration No. 38,898

Date: February 24, 2004  
HALE AND DORR LLP  
1455 Pennsylvania Avenue, NW  
Washington, DC 20004  
Phone: 202-942-8400